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Identification of human ABCB5$^+$ dermal progenitor cells with multipotent differentiation plasticity

S Kim,[1] B Meier,[2] T Schatton,[1] B Wilson,[3,1] Q Zhan,[3] YH Loh,[1] GQ Daley,[1] MH Sayegh,[3,1] Y Ziouta,[4] C Ganss,[4] K Scharffetter-Kochanek,[2] GF Murphy,[3] MH Frank[1,3] and NY Frank[5,3,1] *1 Children's Hospital Boston, Boston, MA, 2 University of Ulm, Ulm, Germany, 3 Brigham and Women's Hospital, Boston, MA, 4 TiCeBa GmbH, Heidelberg, Germany and 5 VA Boston Healthcare System, Boston, MA*

Skin stem cells posses promising therapeutic potential. Here we report identification of a novel skin-associated cell population based on expression of the ATP-binding cassette transporter, ABCB5, which is found in and can be isolated from the dermis of healthy humans or human patients. ABCB5$^+$ skin cells reside in the reticular dermis, can co-express the stem cell marker CD133, and are distinct from CD31$^+$ stromal cells and CD34$^+$ dermal cells. Comparative analysis of early developmental and lineage-specific gene expression patterns demonstrated ABCB5$^+$ dermal cells to be distinct from mature human fibroblasts, and to exhibit the more primitive molecular phenotype of human fibroblast-derived induced pluripotent stem (iPS) cells, and of human embryonic stem (ES) cells, with respect to down-regulated expression of vascular endothelial differentiation markers. In differentiation assays, purified ABCB5$^+$ dermal cells were capable of giving rise to all three embryonic lineages (ectodermal, mesodermal and endodermal) *in vitro*. Moreover, in a human to mouse skeletal muscle injury xenotransplantation model, human ABCB5$^+$ dermal cells possessed the capacity to differentiate into human spectrin- and delta-sarcoglycan-positive skeletal myofibers and to contribute to skeletal muscle regeneration *in vivo*. Interestingly, while ABCB5$^+$ dermal cells could be consistently detected in the skin of healthy humans of all ages, a significant decline in ABCB5$^+$ cell frequency was observed in older individuals. Thus, ABCB5 expression defines a novel dermal progenitor cell population in human skin that posseses multipotent differentiation plasticity. These results suggest a physiological role of ABCB5$^+$ progenitor cells in tissue repair and regeneration. Moreover, they point to potential therapeutic utility of purified ABCB5$^+$ dermal cells in regenerative medicine.